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DEPARTMENT OF THE ARMY
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ON OUR 15-YEARS OF EXPERIENCE WITH DEEP MYCOSES

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In our country [Hungary], we have two forms of deep and serious skin mycoses: actinomycosis and blastomycosis. We would like to report here on the 67 cases reported in our clinic since 1949; of these, 39 were actinomyces and 28 were blastomyces infections. In the past, the various regional forms of actonomycosis could be observed predominating among the cases of deep skin mycoses. In our hospital, almost every infection was caused by the anaerobic Actinomyces wolf-israeli. This fungus generally spread rather slowly but it does not produce any wide distribution; this is something which we can certainly confirm, with the exception of only 2 cases. As far as the type of infection is concerned, we might mention the well-known fact that an infection from one human being to the other, respectively, from one animal to another animal generally does not take place here. According to some individual reports, however, the infection can be transmitted from animal to man in some very unusual cases. The infection is generally caused by actinomycetes which reach man from plants. The fungus can be present in an apathogenic form mostly in the mouth and it can then become pathogenic as a result of a number of circumstances which promote this development, such as gradual sensitization, tissue adaptation of the fungus, reduction in tissue resistance, and inflammations caused by various circumstances. Our material, which was under observation since 1949 was arranged in groups from various viewpoints and enabled us to make the following findings: (1) with respect to the location, we had swelling-like changes in the cervico-facial region in 28 cases, in the abdominal region in 5 cases, in the chest and lung region in 3 cases, we had Madura foot in one case, disseminated skin actinomycosis in one case, and actinomycosis in the mustache region likewise in one case. This last change had been caused by Actinomyces griseus; (2) in 39 cases, the individuals infected were mostly farm workers; but other occupations were represented with 1 case, each; these included the following: shepherd, forestry, transportation, industry worker, carpenter, locksmith, soldier, apprentice, musician, etc; (3) as far as the sex distribution was concerned, we found confirmation once again for the well-known observation that the infection is much rarer in women; (4) it was possible to establish the presence of the fungi by means of the microscope or by means of cultures in 23 patients, in other words, 58% of our cases here; 22 cultures revealed the anaerobic Actinomyces

wolf-israeli; and in 1 case we were able to breed the previously-mentioned aerobic Actinomyces griseus globisporus. The intracutaneous allergy test, which was performed on 23 patients, turned out positive in 14 cases, and negative in 9 cases; in the other patients, this test was not performed for various reasons; (5) the complement fixation reactions are quite difficult here because of the fact that we can get a good antigen only in a fresh culture. This explains the low positivity value (8.3%) in the material which we examined; this low figure at the same time also points to the, by the way, generally-known low over-all value [sic]. A comparison between man and animal shows that we find a larger percentage of mouth cavity symptoms in animals than in man. In man, these symptoms were hardly ever observed; nevertheless, our material revealed the secondary cervico-facial skin type, caused mostly by mouth cavity infection. Compared to conditions in man, we also note the large mass of fungus elements, respectively, druses [granules] which can be observed in the pathohistological sections obtained from the animals. The frequency of mouth cavity infections in cattle can perhaps be easily explained by the anatomical structure of the tongue and the fodder which the animals eat. Our patient material revealed generally the customary clinical situation that obtains in actinomycosis. There are 5 cases here which merit special mention. (1) In a 53-year old gardener, an about nut-size, consistent formation had developed on the right side of the mustache; this formation looked like a swelling and contained hardly any pus at all. We were able to breed actinomyces griseus globisporus from the mass surrounding the mustache hair. An infection of this kind, which is caused by this fungus that is known to be apathogenic, had not been known so far. The pathohistological investigation revealed thin threads embedded in granulation tissues. (2) In a 33-year old farm worker, actinomycosis developed on the right foot, starting from the toes; this actinomycosis later on deformed the entire foot, with bone destruction; here we had the characteristic picture of Madura foot. In the secretion, we were able to establish actinomyces-druses whose fungus-elements turned out to be Actinomyces wolf-israeli in the culture. In our domestic case histories here, this was the 4th case. The foot had to be amputated. (3) A 21-year old shepherd fell on his stomach and injured the skin on the stomach. A primary skin actinomycosis developed on the stomach wall, starting from the place of the injury. We were able to breed Actinomyces wolf-israeli from the secretion. The Actinomyces wolf-israeli infections in our patient material, as we said before, were not disseminated, with the exception of 2 cases. Here are more details on these 2 cases: (1) in a 37-year old electrical technician, the primary focus was in the upper lobe of the left lung. After resection, abscesses developed on the back and on the thigh and from these abscesses we were able to breed an actinomyces strain. The cachectic patient recovered after administration of 40 million units of penicillin. This patient was a case at one of our surgical clinics; (2) in a 59-year old farm worker, abscesses had been developing in the skin, in various regions of the body, for 1 year. At the time of admission, we were able to observe dinner-plate sized inflitrates in the region of the appendix, the front surface of the left thigh, above the hollow of the knee, above the left nipple, and on the right-hand gluteus. All of this pus was emptied through fistulas. In both cases we were able to breed Actinomyces wolf-israeli. The treatment we used here was gradually revised, as time went on. At first we used sulfonamides, gold, vaccine, and iodine; then we switched

of penicillin treatment. The daily and the total dose depended on the location, the dissemination, and the duration of the disease. The vast majority of our cases consisted of cervico-facial cases and these healed relatively quickly and the total amount was rather small [sic]. The secondary skin infections of visceral origin healed less quickly and less definitely. The Madura foot had to be amputated. We did not lose any patients at our clinic, however. From the therapeutic viewpoint, we might also mention vitamin K whose inhibitory effect on certain fungus strains was confirmed by Nekam. On the basis of these observations, infiltrations of vitamin K were made into the swelling-like, actinomycotic changes in the chin lobe of cattle. It was interesting to note how quickly the fungus elements, respectively, druses disappeared from the histological section. The intravenous experiment in man produced vein spasms and this is why this type of treatment was discontinued. The number of actinomycoses decreased considerably in the skin disease department. Of course, this may partly be due to the fact that the stomatological and surgical departments take over some of the patients; nevertheless, the decrease seems to have been a general one here. Our blastomycosis material looks particularly interesting here. We might supply some further information in this connection concerning one form which seems to be rather on the increase in Hungary. Since 1946, we have been noticing patients at our clinic in whom the changes were always gluteal and perianal. In symptomatological terms it was interesting to note that we had some individual and also several deep subcutaneous-cutaneous knots or nodes in these regions which later on formed extensive infiltrates and which released pus through fistulas but which did not become ulcerous. Another characteristic observation was that the fistulas were connected deep down with each other by means of canals; when pressure was applied on the infiltration in one spot, there was usually a rather large quantity of pus that would suddenly, all at once, drain out through several fistulae. In the patients under observation here, the disease had been taking its course for a number of years and had in most instances been treated as tuberculosis or pyodermia. In quite a number of cases, no diagnosis was made in advance. The clinical picture did not look like anything we had ever seen before. This was why we considered the possibility of a deep fungus infection and this is why we began our investigations along these lines. The proof of fungus etiology was rather difficult to come up with here because a number of accompanying bacterial infections had developed over a period of time and because certain treatments had been administered in advance here. In each case, we tried to establish the presence of the fungus microscopically, culturally, as well as by means of animal inoculations. We fell back on pathohistological findings only [illegible] on the abovementioned investigations produced a negative result [illegible] excision required for pathohistological investigation in several cases could not be performed first of all because of the pus formation and second, because the patients refused to have this done. Intracutaneous tests were made for diagnostic purposes and in the interest of any possible future vaccine treatment. By way of experiment, we also made complement fixation reactions which however could not be used for diagnostic purposes. Our investigations show that one cannot always insist on the fulfillment of all laboratory conditions in diagnosis. It may happen that the diagnosis will be based only on a few positive laboratory results -- results which only serve to reinforce the characteristic symptoms. Now and then we also had to take a position in this respect on

the basis of the characteristic clinical symptoms. Although we did not use the diagnostic method of "ex juvantibus" in fungus infections, we do want to say, in this respect, that antibiotics-resistant symptoms of this kind can arouse suspicion as to fungus infection. When we published our first 15 cases on clinical and laboratory observations (1954), there were a few cases included in which the laboratory investigations did not work out and in which we had to make decisions on the basis of the clinical symptoms. At that time we expressed our viewpoint -- based on clinical and laboratory experiences -- for the first time, to the effect that one not only can make a decision but one sometimes is actually forced to make a decision on the basis of the clinical symptoms in the interest of the patient. In this respect we had two cases which we will mention later on and which turned out to be particularly convincing; these patients reached us after their cases had lasted 23, respectively, 26 years. From one of these cases we bred Cryptococcus neoformans and in the other we were unable to establish any budding fungi. In the latter case we were able to establish Cryptococcus neoformans pathohistologically only as a result of the deep skin excision performed in connection with obduction. We observed a total of 28 such budding fungi produced by deep mycoses here. Of this number, 24 were gluteal and 4 were located elsewhere. In connection with the latter, we were able to observe circumscribed symptoms in 3 patients on the lower arm, the face, respectively, the stomach wall and in one case we had diffuse phenomena on the upper arm. With respect to occupational breakdown, these were farm workers, masons, one agricultural college instructor, factory workers, railroad workers, locksmiths, engineers, civil servants, and housewives [domestic servants].

One thing that struck us particularly was this: in most of the patients under investigation, the symptoms had existed for at least 3 years but we also had cases in which they had existed for 10 years and as much as more than 20 years. An another characteristic thing was the fact that the symptoms had remained localized in spite of the long duration. Only 2 of those patients, in whom the symptoms had existed 23, respectively 26 years, died. In one of these patients, the cause of death was the carcinoma which had developed in the pathological region; in the other case, the cause of death was a general amyloidosis, respectively, nephrocirrhosis, which had been brought about by this long illness. In neither of these 2 cases could we establish any metastases coming from fungi. These observations might perhaps indicate that this form, which is located on the skin, is comparatively nonmalignant because we so far lost only these 2 patients. Of the 24 gluteal processes, a more detailed description of one hitherto unpublished case would appear to be of some interest. The illness of this 61-year old man lasted 18 years. The nodular infiltrates, which later on flowed together, became abscesses, and were accompanied by fistula formation, began in the gluteal region on the one side and also in the perianal region. He was admitted to our clinic in 1962, during the 16th year of his illness; through pathohistological investigation we were able to establish fungus elements imbedded in the cutaneous and subcutaneous tissue and in the granulation tissue. At that time we were able to reduce the infiltration quite considerably and to close the fistulas up by means of internal and local vitamin K therapy. After his discharge, we did not see the patient again until August 1964, when he was brought in in a rather serious condition.

The 4th and 5th segments of the sacrum as well as the Os coccygeum had been destroyed and we could see a fist-sized, irregularly bordered ulcer 'abscess' with necrotic base. The embryonic rectum opening and its surroundings had been necrotized in an area about the size of a dinner plate. The stool was completely emptied into the small pelvis. At admission time, this extremely emaciated, cachectic, and somnolent patient had fever and there were also symptoms of circulatory insufficiency. The pathohistological investigation revealed a spinocellular carcinoma. The patient died 3 weeks after admission. The obduction revealed parenchymatose degeneration. Among the cases discussed we also observed one previously-mentioned case with a quite similar development; here the same situation developed during the 23rd year of the illness and the case likewise ended in the patient's death. Among all of these patients we only had one woman. Summarizing our laboratory investigations we can say this: from the 24 gluteal cases, we were able to breed Cryptococcus neoformans in 4 cases, Candida albicans in 5 cases, Candida krusei in 1 case, and Geotrichum matalense in 1 case. In 15 cases we were able to establish the presence of budding fungus elements through histological examinations; in 3 cases the histological examination was negative; in 6 cases no such examination or investigation was performed. Of the 11 cases, which were negative with respect to the fungus culture, 7 turned out to be histologically positive. In this way, the culture was positive in 13 out of 24 cases; in 7 cases, histological investigations helped in our diagnosis while in the other 4 cases we were helped by other circumstances (deep excision during obduction, clinical symptoms, allergy tests). In the non-gluteal locations, the histological results and the cultures shaped up somewhat like this: we were able to breed Actinomyces wolf-israeli from the stomach wall changes of the first case, which were located in the area of the caecum; upon histological investigation, we found budding fungus elements embedded in the deep cutaneous tissue, in typical granulation tissue; in this case we were dealing with the simultaneous occurrence of two fungus varieties. In the second case, we were able to observe changes of the Busse-Buschke type in the upper extremities; from these substances we were able to breed Cryptococcus neoformans; and we were also able to establish budding-fungus elements in the pathohistological section. In the third case, a phlegmonous condition developed along the lower arm 'underarm' of a wire-drawing worker due to an injury; this condition lasted for many months and led to the formation of fistulas. A Torulopsis strain could be bred from the change; we were able to establish the presence of budding-fungus elements also in the deep cutaneous tissue. In the 4th case, the change was located in the face; it corresponded to a blastomycosis of the Gilchrist type; the ulcerating process, which featured micro-abscesses on the edge, spread to the nose ridge and to the forehead; from here we were able to breed Candida albicans. With respect to the gluteal deep blastomycosis here we were able to establish that this form of disease can be caused not only by Cryptococcus neoformans but also by other budding fungi. We had no reason to expect any results from the complement fixation reaction and we therefore generally refrained from performing it. The skin specimens turned out to be positive in 16 out of 24 cases. The blood count drop in most of the gluteal cases was increased, mostly around 60 and now and then above the value of 100 mm/hr. As far as the qualitative and

quantitative aspects of the blood report were concerned, we generally could not observe any major deviations. The patients generally had no fever. Minor temperature increases were recorded now and then. In some patients there was higher fever temporarily at the time of abscess formation.